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Beyond Acetylene: Exploring Solvent Stabilization of Calcium Carbide-derived Acetylide Intermediates and Their Significance in Small Organic Molecule Synthesis

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The reaction of calcium carbide with water has been widely used as a source of acetylene for the synthesis of organic molecules. In contrast with this traditional approach, we use the CaC_2 reaction under water-starved conditions and show reactions that involve a calcium acetylide intermediate, reminiscent of Grignard reaction intermediates, which are stabilized by the solvent. Using this reaction pathway may allow for new chemistry, finer reaction control, and safety by limiting the formation of acetylene gas during the reaction. For example, reaction with bromoarenes, readily yields the corresponding diaryl acetylene.

Introduction

Calcium carbide has long been used as a convenient precursor for acetylene (reaction 1) which can be generated locally in small amounts, thus avoiding the explosion-risk associated with storage of large quantities of acetylene.

$$CaC_2 + H_2O \longrightarrow Ca(OH)_2 + C_2H_2 \qquad (1)$$

This work focuses on determining whether the detection of carbide intermediates can provide a better understanding of the role of calcium carbide in organic synthesis, thereby inspiring new applications. Specifically, if the reaction of calcium carbide in water-starved conditions primarily involves partial hydrolysis to soluble intermediates that may have benefits over typical full hydrolysis to acetylene.

In many cases reaction 1 is performed *in situ* as a convenient and safe precursor of C_2H_2; in this case the chemistry involved is simply that of acetylene with the added convenience of local generation, and can be used in a variety of different synthetic processes.[1,2] Reactions include copper click chemistry,[3] Sonogashira-like formation of symmetrical diarylethynes,[4–9] and ethynylation of aldehydes and ketones.[10] *In situ* C_2H_2 can also be used as a precursor for vinyl derivatives,[11,12] including with ^{13}C substitution.[13]

In the last few years calcium carbide has been explored under water-free conditions as a potential precursor for electronic materials such as graphyne[14] or triazine structures;[15] while not the target of these reports, some studies observed the formation of some small molecule by-products preserving the alkyne moiety. There have also been studies into symmetric diaryl ethyne synthesis under water-starved conditions, where undried solvents supplied adequate water to initiate the catalytic cycles.[2,5] However, these examples typically behave the same, or are improved, with added water.

In this contribution we report that under controlled thermal conditions and low water content in dimethyl sulfoxide (DMSO), it is possible to direct the chemistry of CaC_2 towards the formation of acetylide intermediates in solution. We examine the formation of this intermediate using DMSO as a solvent in an example reaction: this intermediate can be used to facilitate the formation of symmetrical diarylethynes using Pd deposited on TiO_2 as a catalyst (reaction 2).

$$\begin{aligned}&CaC_2 + H_2O \xrightarrow[DMSO]{} HC{\equiv}C{-}CaOH\\&\xrightarrow[2R\text{-}X]{Cat} RC{\equiv}CR + CaX_2\end{aligned} \qquad (2)$$

It is interesting to think that if the acetylide chemistry observed here can be expanded to a fraction of what Grignard reagents can do, then there is bright future for CaC_2 under water-starved conditions.

Results and Discussion

Our studies concentrate in water-starved systems, where the chemistry observed is different from that of just acetylene, regardless of whether this is generated *in-situ* or not. We are also more interested in mechanistic aspects than in expanding the scope of the system examined here. We can illustrate our

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approach with a very simple system used here as a tool for mechanistic studies, diphenylacetylene (tolan) can be prepared from CaC_2 and bromobenzene, reaction 3, using a catalyst based on Pd deposited on TiO_2 (Pd@TiO_2).

$$CaC_2 + 2PhBr \xrightarrow[140\,^{\circ}C]{Pd@TiO_2} \underset{\mathbf{P1}}{Ph{-}C{\equiv}CH} + \underset{\mathbf{P2}}{Ph{-}C{\equiv}C{-}Ph} + CaBr_2 \qquad (3)$$

Pd@TiO_2 has proven effective before in the photocatalysis of the Sonogashira reaction[16,17] that also involves couplings of alkynes, however, reaction 3 is a thermal process. Here the reaction can be catalysed thermally whereas no activity is observed under visible light excitation at room temperature. After initial investigations (see Supporting Information), overall standard reaction conditions were decided upon, then applied for further modification, including a few other substrates, and mechanistic analysis.

Kinetic studies suggest the reaction reaches a maximum yield of diphenylacetylene (P2) after 4 h of heating at 140 °C. There is also an initial formation of phenylacetylene (P1), reaching a maximum after 1 h, before being converted to the final diphenylacetylene product (Figure S1). Only small traces of unreacted bromobenzene were present at the end of the kinetic studies. The loss of some bromobenzene is likely due to dehalogenation to benzene along with some adsorption onto the catalyst.

The reaction conditions (Cs_2CO_3 and CaC_2) were then optimized to maximize the yield of P2 (see Table 1). It appears that optimal yields of P2 require between 2.5 and 5 equivalents of Cs_2CO_3 as a base, and 5–10 equivalents of CaC_2. Using additional CaC_2 can also negatively impact the reaction (see Table 1, entry 7), perhaps through the formation of larger conjugated carbon structures such as graphyne.[14] The best yield of P2 was observed in entry 6, which will be used as the standard conditions moving forward. Dimethylformamide (DMF) was also tested as an alternative polar aprotic solvent (see Table 1, entry 10), which led to no formation of products. This implies DMSO is an important part of the reaction. The Pd@TiO_2 catalyst is also required for the formation of product, as shown in entry 8 with no product being formed in its absence. Pd@SiO_2 was also tested as an alternative catalyst (see Supporting Information, Table S1), and showed greatly reduced yields. Similarly, six other coupling reagents were tested; among these 3-bromopyridine and 4-bromotoluene gave yields in excess of 44 % (Table S1).

Table 1. Optimization of reaction conditions for synthesis of diphenylacetylene (P2), with optimal conditions in bold.

Entry	Cs_2CO_3 (eq)	CaC_2 (eq)	Other	% Yield (Error)[a]	
				P1	P2
1	2.5	5	–	10.0 (5.3)	44.5 (5.7)
2	5	5	–	11.3 (0.5)	47.0 (0.5)
3	1.2	5	–	8.0 (0.2)	38.8 (1.5)
4	0.6	5	–	10.2 (0.6)	18.2 (0.4)
5	2.5	1.2	–	3.9 (1.5)	9.2 (8.5)
6	**2.5**	**10**	–	**8.4 (0.6)**	**48.3 (2.4)**
7	2.5	20	–	9.4 (4.0)	21.7 (0.6)
8	0	10	–	0	0
9	2.5	10	No catalyst	0	0
10	2.5	10	In DMF	0	0

Reaction conditions: bromobenzene (0.1 mmol), CaC_2, Cs_2CO_3 base, Pd@TiO_2 catalyst (20 mg), DMSO solvent (5 mL), argon atmosphere, 140 °C, 4 h.

[a] Yields evaluated by GC-FID using *trans*-stilbene as external standard.

The initial experiments in Table 1 were conducted with undried DMSO straight from the bottle. Reported studies of the water content of DMSO, suggest that on average it contains 0.1 % water,[18] corresponding to about 5 μL or 0.25 mmol in the 5 mL of solvent used. Prior studies have shown that small amounts of water can be used catalytically with CaC_2 as a precursor, thus evaluating the effects of water content is necessary.[5] Reactions with various amounts of added water were conducted, as well as with DMSO dried with molecular sieves. Table 2 shows that small amounts of water, up to 20 μL, can facilitate the reaction, however, excess water appears to poison the reaction preventing formation of the product. Thus, 200 μL of added water (see Table 2, entry 5) showed no formation of either product. If the reaction simply involved generation of C_2H_2 by reaction with water, we would expect water to directly facilitate the reaction; this is clearly not the case, indicating that there is more than making C_2H_2 to the mode of action of CaC_2 under these conditions.

Suspecting that the reaction involved more than the simply *in situ* generated C_2H_2, we decided to explore a two-step methodology that would minimize the reaction of gaseous or dissolved C_2H_2. The first step involves heating CaC_2 in DMSO to attempt to preload the solvent with a reactive soluble intermediate. After removing any solid material, this mixture was then reacted with bromobenzene under standard con-

Table 2. Effect of water content on the yield of diphenylacetylene (P2).

Entry	Water volume added	% Yield[a]	
		P1	P2
1	5 μL	16.6	43.7
2	10 μL	17.0	33.1
3	20 μL	13.5	42.0
4	50 μL	11.5	21.4
5	200 μL	0	0
6	0 μL[b]	18.1	35.4

Reaction conditions: bromobenzene (0.1 mmol), CaC_2, Cs_2CO_3 base, Pd@TiO_2 catalyst (20 mg), DMSO solvent (5 mL), argon atmosphere, 140 °C, 4 h.

[a] Evaluated by GC-FID using *trans*-Stilbene as external standard.

[b] Dry DMSO.

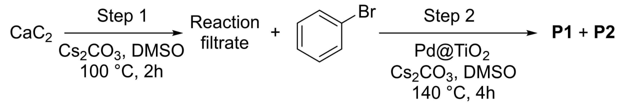
ditions, without the addition of more CaC_2. Significant yield of the expected products would imply a soluble, non-gaseous intermediate of CaC_2. The results of this two-step approach are shown in Table 3.

Examination of Table 3 and comparison of the yields with Table 1 suggests that a highly reactive species is transferred in the filtrate solution between the two steps. Entry 1 shows a yield of 29.9% for P2, lower than the one observed in the equivalent one-step reaction (entry 6, Table 1), but significant. Not much C_2H_2 is likely to remain in solution, particularly given the high working temperatures and the anticipated reduced solubility under these conditions.[19] Therefore, the reactive species transferred between the two steps is unlikely to be simply C_2H_2 gas. We propose that the transferable intermediate is a calcium acetylide, most likely species **1**, but possibly **2**, during a one-step reaction, given the presence of bromide in the system.

$$\underset{\mathbf{1}}{H{-}{\equiv}{-}CaOH} \qquad \underset{\mathbf{2}}{H{-}{\equiv}{-}CaBr} \tag{4}$$

The structures of species **1** and **2** are clearly reminiscent of Grignard reagents, and their reactivity with bromobenzene seems to follow a typical carbanion-like type of behaviour. Similar species have been suggested and calculated before, with one providing a mass-spectrum of the ethynyl calcium hydroxide intermediate.[5,20–22] Confirmation of structure **1** was attempted by NMR and electrospray ionization mass spectrometry (ESI-MS) (Figures S2–S7). The ^1H NMR spectrum shows a peak (*ca.* 3 ppm) corresponding to a small amount of acetylene in solution and a more prominent one at 2.84 ppm, which can be attributed to a different hydrogen atom than those found in acetylene. Signals also disappear after additional mixing with water, as expected with conversion of product **1** (Figure S5). ^{13}C NMR only shows signals from the carbon of the terminal C–H. In deuterated DMSO, the introduction of a triplet peak indicates some degree of proton exchange with the solvent. The lack of a peak corresponding to the carbon bound to –CaOH is due to the greatly reduced signal intensity of un-protonated carbons, and the overall low concentration of the intermediate. As expected, ESI-MS also showed the introduction of a signal with a molecular weight of 105, corresponding to the $M+Na^+$ peak of ethynyl calcium hydroxide previously observed in literature.

Table 3. Optimization of conditions for two-step reactions.



Entry	Step 1 Changes	Step 2 Changes	% Yield[a]	
			P1	P2
1	None	None	15.2	29.9
2	Pd@TiO_2	None	13.7	55.5
3	Pd@TiO_2	No Pd@TiO_2	11.0	47.9
4	None	No Pd@TiO_2	0	0
5	5 μL H_2O	None	10.6	35.53
6	10 μL H_2O	None	10.6	52.9
7	No CaC_2	None	0	0
8	10 μL H_2O; no Cs_2CO_3	None	11.6	49.2
9	10 μL H_2O; 60 °C	None	15.2	44.5

Reaction conditions: Step 1. CaC_2 (10 eq), Cs_2CO_3 base (2.5 eq) DMSO solvent (5 mL), argon atmosphere, 100 °C, 2 h. Step 2. Cs_2CO_3 base (2.5 eq), step 1 filtrate as solvent (5 mL), Pd@TiO_2 catalyst (20 mg) argon atmosphere, 140 °C, 4 h. [a]Yields evaluated by GC-FID using *trans*-stilbene as external standard.

Adding small amounts of water during the first step enhances the reaction to yields comparable with the optimized one-step reaction (Table 3, entries 5–6). The two-step reaction requiring some additional water is expected as it cannot use the water catalytically. The acetylide intermediate transferred between the two steps cannot be remade in step two, which makes it more water dependent. Pd@TiO_2 catalyst can also be added in the first step instead of additional water to achieve similar yields. Interestingly, the second step can be run in the absence of the catalyst. This may suggest soluble Pd species can be transferred to the second step and may not be an entirely heterogeneous process. We note that no Pd was detected in ICP studies, suggesting that if present the amount transferred must be below our detection limit of <0.05 ppm. The first step can also be conducted in milder conditions without the presence of base, or at temperatures as low as 60 °C. No product is detected if the catalyst or CaC_2 is missing in both steps of the reaction.

Experimental Section

Materials

All reagents used were purchased from Sigma Aldrich and used as received. TiO_2 P25 was purchased from Univar Canada.

Quantification of products was conducted in a Perkin Elmer, Claurus Gas Chromatograph coupled to a Flame Ionization Detector (FID). Confirmation of the products was performed by mass spectrometry in an Agilent 6890-N Gas Chromatograph with an Agilent 5973 mass selective detector calibrated with acetophenone. ^1H NMR and ^{13}C NMR spectra were recorded in a Bruker Avance 300 expressing chemical shifts in ppm relative to the H (or C) of the solvent (d_6-DMSO). ESI-MS was conducted with an Agilent InfinityLab Liquid Chromatograph/Mass Selective Detector (single quadrupole detector), with sample injected directly into the MSD.

Catalyst Synthesis

The catalyst Pd@TiO_2 was prepared photochemically as in earlier reports[23] giving a Palladium mass loading of 2%, and particle size of ~1.6 nm. In short, this was done photochemically by irradiation of a sonicated mixture (20 min sonication) of P25 TiO_2 and $PdCl_2$ salt in MilliQ water with a theoretically mass loading of 2.5%. Irradiation was conducted for 8 h by 14 UVA bulbs in a photoreactor with constant stirring. The irradiated TiO_2 reduces Pd(II) to form nanoparticles on the surface.

One-Step Reaction System

For a typical reaction 0.1 mmol of bromobenzene was added to 5 ml of DMSO with 0.25 mmol of Cs_2CO_3, 1 mmol of CaC_2 and 20 mg Pd@TiO_2 catalyst (Cs_2CO_3 and CaC_2 amounts were varied as noted). To purge with argon, vials were put into a glove bag and put through repeated cycles of removing gas under vacuum and filling with Argon (4 cycles total) and then closed the vials while in the glovebag giving an argon headspace. If water is added to the reaction, it is added in the glovebag before tightly closing the vial. The vial was then heated at 140 °C for 4 hours in an oil bath with constant stirring.

Two-Step Reaction System

One mmol of CaC_2 was added to 5 ml of DMSO, with or without Cs_2CO_3 and Pd@TiO_2 catalyst. Was purged as mentioned in the one-step reaction system then heated at 100 °C (or as otherwise noted) for 2 hours. The reaction mixture was then centrifuged at 10,000 rpm for 10 min to remove solid material. The resulting filtrate was then used as a replacement to the DMSO in a normal one-step reaction setup (without additional CaC_2 being added.

Product Analysis by GC-FID

Reaction mixture was diluted with water and extracted 3 times with hexane. Trans-stilbene was added as an external standard and the concentrations of residual bromobenzene and products P1 and P2 were evaluated by GC-FID. Products identities were also confirmed by GC-MS analysis.

Conclusions

Overall, we have shown the use of DMSO as a solvent to stabilize solubilized intermediates of CaC_2 in solution for use in Sonogashira-like reactions such as the synthesis of diphenylacetylene from bromobenzene. Intermediates such as ethynyl calcium hydroxide have been proposed in the past, however had not been adequately evaluated through mechanistic analysis. The use of a two-step reaction has adequately confirmed the transfer of a soluble reactive species, as well as the stability of the species in solution over short periods of time. Loading the DMSO with these soluble species may also allow for finer control of reactive acetylenic compounds in solution, even allowing for asymmetric additions.[24] We believe that the initial 'loading' of DMSO with these reactive species opens up a new controlled approach to calcium carbide based acetylenic chemistry. This method may be applicable in many other synthetic systems involving alkynes, as well as with other catalysts (both homogeneous and heterogeneous).

Supporting Information Summary

Supporting Information includes kinetic plots, Mass spec and NMR data.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Palladium catalysis · Acetylide intermediate · Catalysis · and Calcium carbide

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